REMARKS

Reconsideration is requested.

The Examiner interview of December 1, 2005 is acknowledged, with appreciation. The Examiner interview is accurate in its brief statement of the issues discussed.

Claims 25, 27, 29, 31, 35, 37, 39, 41, 45, 47, 49, 53, 55 and 57 will be pending upon the entry of the present Amendment. Claims 1-24, 26, 28, 30, 32-34, 36, 38, 40, 42-44, 46, 48, 50-52, 54 and-56 have been canceled, without prejudice. The claims have been amended to advance prosecution, without prejudice.

The Section 112, first paragraph, rejection of claims 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54 and 56 stated in the 3rd paragraph of the Office Action dated September 23, 2005, will be moot upon entry of the present Amendment. Entry of the present Amendment is requested therefore to, at a minimum, reduce the issues for appeal.

The Section 112, first paragraph "enablement", rejection of claims 24-57 stated on pages 2-4 of the Office Action dated September 23, 2005, is traversed. Reconsideration and withdrawal of the rejection are requested in view of the following further comments.

A similar rejection, although within the context of Section 112, first and second paragraph rejections, has been made by the present Examiner in the applicants co-pending application Serial No. 08/362,455. The applicants submitted the following analysis in response to the rejection in the copending application, which is repeated here for completeness.

The applicants submit that one of ordinary skill in the art would be able to make and use the claimed invention without undue experimentation.

Upon entry of the present Amendment, the claims will not require hybridization, as suggested by the Examiner as a basis for the rejection. The present claims relate, in part, to HCV polynucleic acids consisting of at least 8 contiguous nucleotides of specifically recited sequences. The claim structure and recitation of at least 8 contiguous nucleotides is, in many respects, the same as the claims of U.S. Patent No. 6,762,024, which the present Examiner found enabled by the contents of the present specification.

As discussed with the Examiners during the interview, the claims further require the presence of at least one genotype-specific nucleotide. The specification, including the Figures, describe genotype-specific nucleotides required by the claims.

The identification of the genotype-specific nucleotides of the claims will be demonstrated further below by analyzing the polynucleic acid sequences of the disclosure. The Core/E1 region was chosen in the following analysis as the more difficult example to perform a detailed analysis of how to determine genotype-specific nucleotides in the nucleotide sequences as claimed. A similar analysis could be done for the Core region of HCV subtype 3c, as in the present application. However, the applicants believe that the analysis performed in the co-pending application and represented below should be sufficient to convince the Examiner in the present application that the claims are supported by an enabling disclosure which adequately describes the claimed invention.

On page 3 of the Office Action September 23, 2005, the Examiner refers to references of Kennell (1971) and Wallace (1987) as a basis for asserting that the specification allegedly fails to enable the claims. A similar rejection was advanced by the present Examiner in the related application which issued as U.S. Patent No. 6,762,024.

As noted to the Examiner prior to issuance of the related U.S. Patent No. 6,762,024, the fragment of Wallace et al. quoted by the Examiner does not exclude the possibility that probes shorter than 14 bases can be found suitable for specific hybridization, see, the wording "tendency" and "probably" in said fragment. Wallace et al. further specify that the specificity of a probe should first be determined (lines 7-8 on page 434).

In support, the applicants submit the attached two examples of successful use of probes or primers shorter than 14 nucleotides. Specifically, Majzoub et al. (1983, PNAS 258, 14061-14064; of record) successfully utilized 8-mer primers, and Chan et al. (1979, PNAS 76, 5036-504; of record) successfully utilized 10-mer probes.

Moreover, as discussed with the Examiners during the interview, genotype specific differences e.g. between HCV subtype 1a and 1b, can be detected based on probes with a difference of only 1 nucleotide. The specification, including the Figures, describe genotype-specific nucleotides required by the claims.

As also explained by the inventor during the interview with the Examiners, the definition of genotypes and subtypes of the claims are well understood from the present specification (more specifically, see pages 8 to 10) and generally advanced level of skill in the art (more specifically, see summary of the art in Table 3 on page 11 of the specification).

The requirement for a genotype-specific nucleotide, not only distinguishes the claims over the art but may also provide distinctions in identification, treatment and disease outcome, for example, as discussed with the Examiners during the interview. For Example, determination of HCV genotype is currently mandated by the FDA prior to determination of the duration of interferon/ribavirin treatment.

The following examples of genotype/subtype specific nucleotides in Core/E1 region are further provided from the specification, by way of example.

The specification describes genotype-specific amino acids in the new HCV amino acid sequences of the invention, see penultimate paragraph on page 4. The specification further teaches that, at the nucleotide level, additional genotype-specific residues are discerned due to the fact that not all differences in nucleotide sequence are translated into differences in amino acid sequence, as will be expected by one of ordinary skill in the art. See penultimate paragraph on page 3.

The specification moreover discloses amino acid sequence regions (9 to 14 consecutive amino acids in length) that in fact are specific to an HCV genotype or subtype, see pages 35-38. The ordinarily skilled person will understand from this that genotype-specific nucleotides can be determined in the same manner as genotype-specific amino acids.

At the suggestion of the Examiners during the interview, the applicants also demonstrate in the following analysis that the written description of the present application provides ample basis for the claimed invention which recite at least one genotype-specific nucleotide.

For this analysis, the Examiner is referred to the following reproductions of the Figures of the application. Specifically, the following are a duplicate of pages 26/111 to 49/111 of Figure 4 of the present application with additional sequence information relating to sequences PC-3-4, PC-3-8, PC-2-1, PC-2-6 and PC C/E1 from Figure 9 of the application having been added in hand-written text for he convenience of the Examiner. This following reproductions provide an alignment of the nucleotide sequences of different HCV subtypes (subtype 2d, subtype 3a, type 4, subtype 5a isolates) with known sequences from the corresponding region of type 1 and type 2 and type 3. This region, i.e., the Core/E1 region is, in comparison with other coding sequence regions, relatively well conserved and was therefore elected as the more difficult example to perform an exemplary analysis of the description of genotype-specific nucleotides in the nucleotide sequences of the claims and specification.

Nucleotides at a certain position from a sequence with a given SEQ ID NO (i.e. representing a specific subtype) differing from other nucleotides of known or new subtypes at the same position in the alignment are considered genotype-specific nucleotides. Vertical lines are meant to promote reading of the aligned sequences. The applicants believe that this analysis is described in the specification and can be performed by one of ordinary skill in the art to, for example, delineate a region of at least 8 contiguous nucleotides containing at least one genotype-specific nucleotide, around the genotype-specific nucleotides indicated in the following, and more generally, in all other claimed sequences.

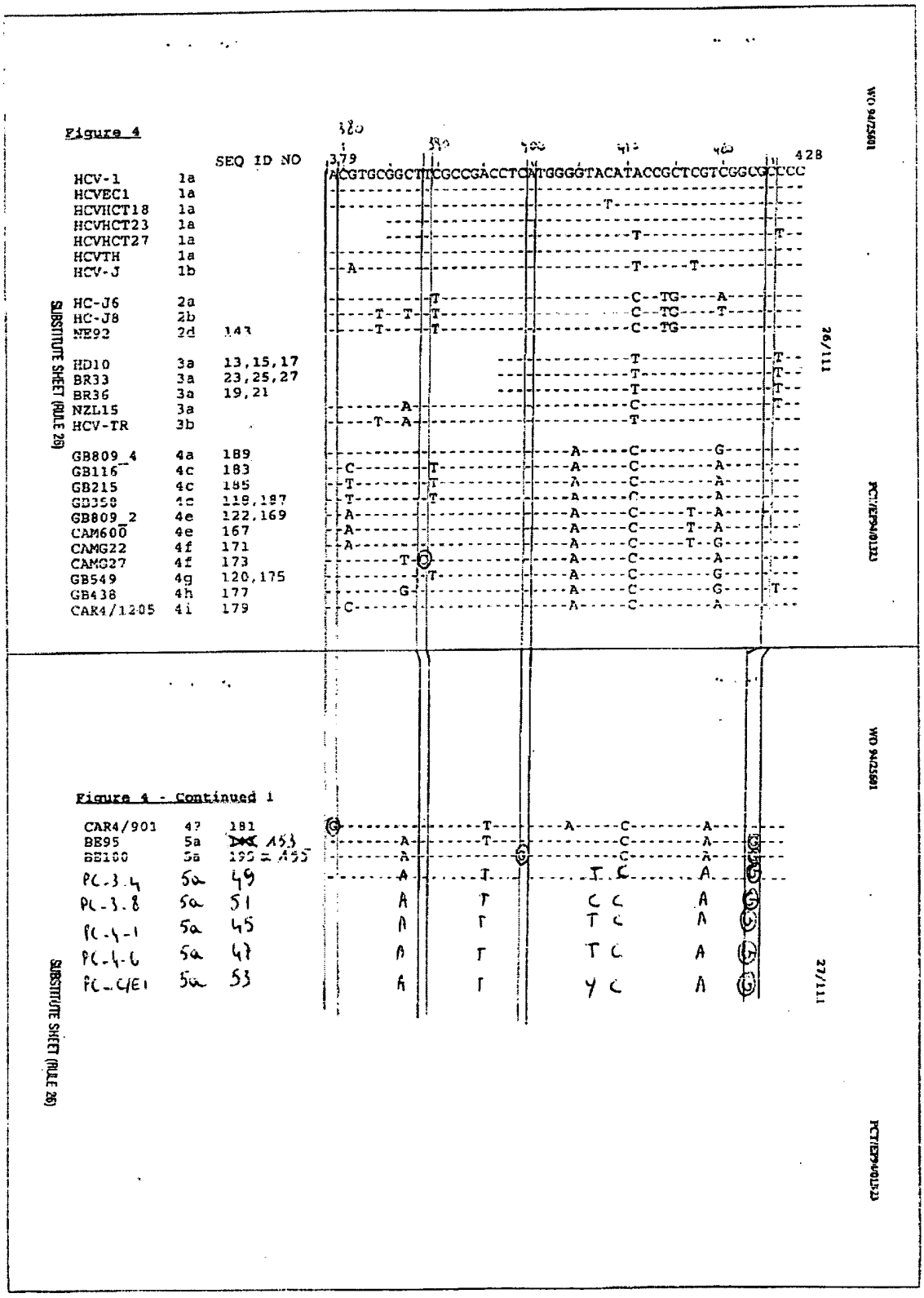
Figure 4
SEQ ID NO
HCV-1 1a
HCVEC1 1a
HCVHCT18 1a
HCVHCT23 1a
HCVHCT27 1a
HCVTH 1a
HCV-J 1b
HC-J6 2a
HC-J8 2b
NE92 2d 143
HD10 3a 13,15,17
BR33 3a 23,25,27
BR36 3a 19,21
NZL15 3a
HCV-TR 3b
GB809_4 4a 189
GB116 4c 183
GB215 4c 185
GB359 4c 119,187
GB809_2 4e 122,169
CAM600 4e 167
CAMG22 4f 171
CAMG27 4f 173
GB549 4g 120,175
GB438 4h 177
CAR4/1205 4i 179
379
428
SUBSTITUTE SHEET (RULE 26)
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PCT/EP94/01323
26/111
Figure 4 - Continued 1
CAR4/901 4j 181
BE95 5a ~~163~~ 153
BE100 5a 195 = 155
PC-3.4 5a 49
PC-3.8 5a 51
PC-4-1 5a 45
PC-4-6 5a 47
PC-CHE1 5a 53
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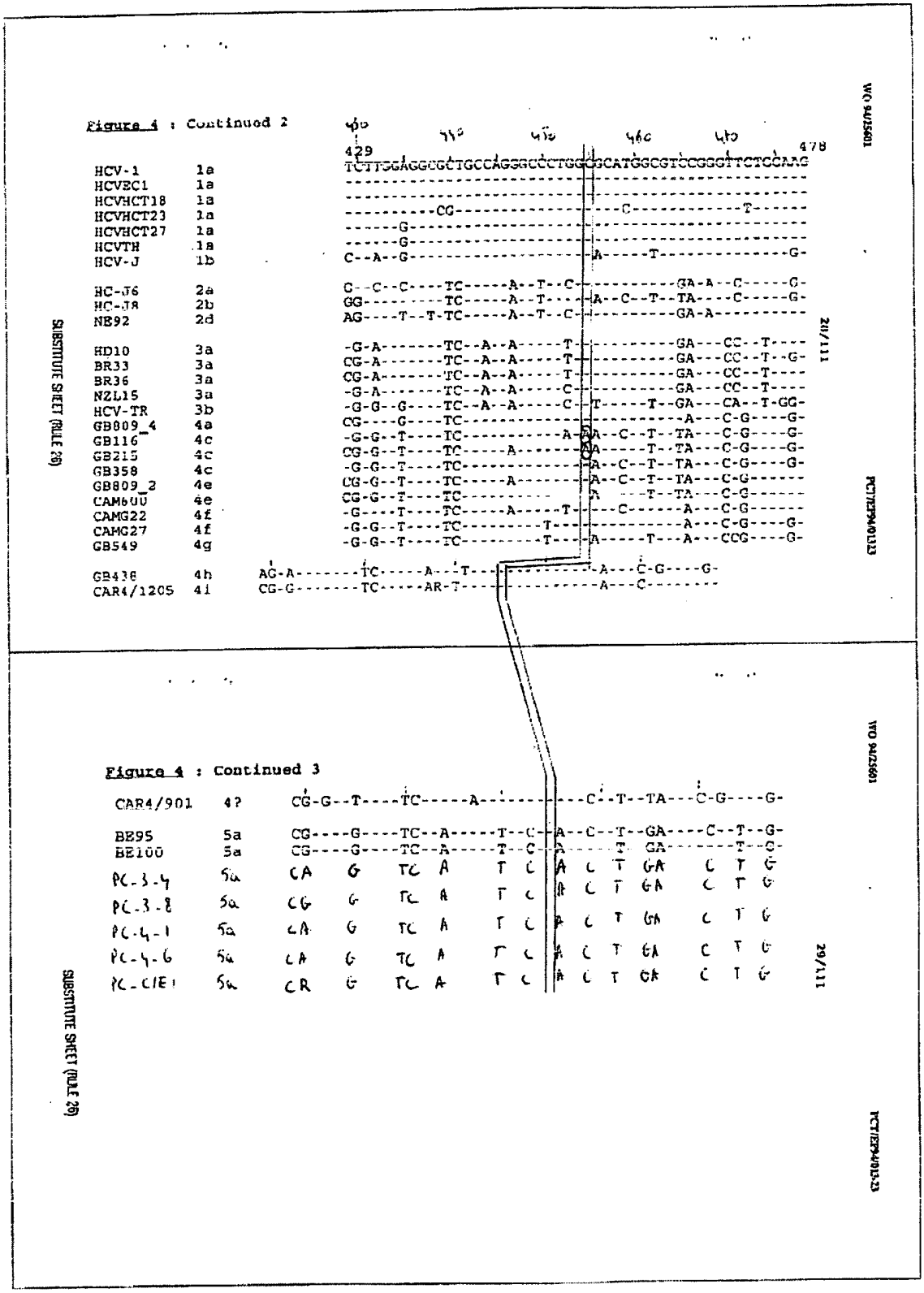
Figure 4 : Continued 2
HCV-1 1a
HCVEC1 1a
HCVHCT18 1a
HCVHCT23 1a
HCVHCT27 1a
HCVTH 1a
HCV-J 1b
HC-J6 2a
HC-J8 2b
NB92 2d
HD10 3a
BR33 3a
BR36 3a
NZL15 3a
HCV-TR 3b
GB809_4 4a
GB116 4c
GB215 4c
GB358 4c
GB809_2 4e
CAM600 4e
CAMG22 4f
CAMG27 4f
GB549 4g
GB438 4h
CAR4/1205 4i
SUBSTITUTE SHEET (RULE 26)
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PCT/EP94/01133
28/111
Figure 4 : Continued 3
CAR4/901 4?
BE95 5a
BE100 5a
PC-3-4 5a
PC-3-8 5a
PC-4-1 5a
PC-4-6 5a
PC-CIE1 5a
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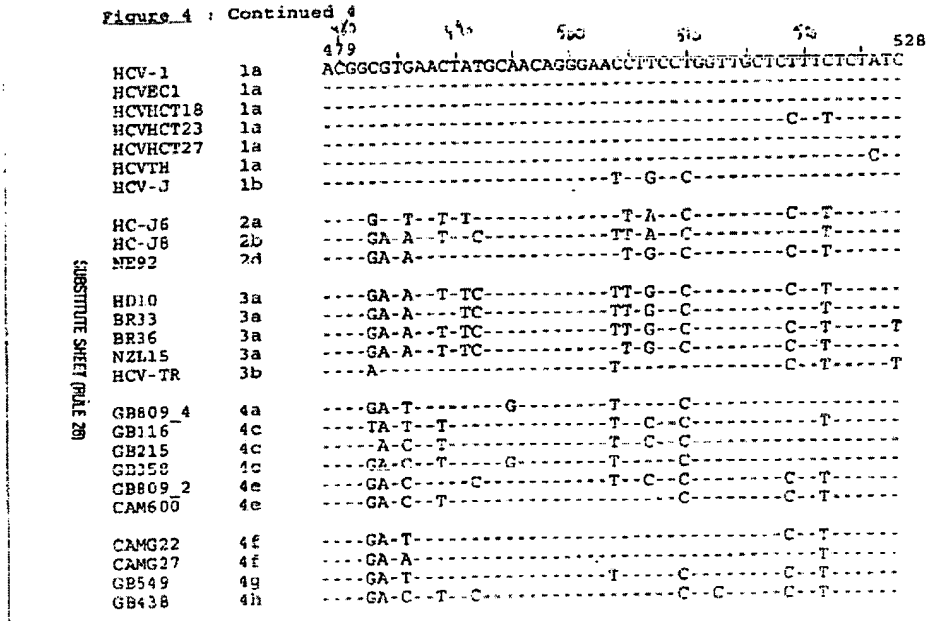
Figure 4 : Continued 4



		479 528
HCV-1	1a	ACGGCGTGAACTATGCAACAGGGAACCTTCCTGGTTGCTCTTTCTCTATC
HCVEC1	1a	----------
HCVHCT18	1a	----------C--T------
HCVHCT23	1a	----------
HCVHCT27	1a	----------C--
HCVTH	1a	----------
HCV-J	1b	----------T--G--C----------
HC-J6	2a	----G--T--T-T----------T-A--C---------C--T------
HC-J8	2b	----GA-A--T--C----------TT-A--C----------T------
NE92	2d	----GA-A----------T-G--C---------C--T------
HD10	3a	----GA-A--T-TC----------TT-G--C---------C--T------
BR33	3a	----GA-A----TC----------TT-G--C----------T------
BR36	3a	----GA-A--T-TC----------TT-G--C---------C--T-----T
NZL15	3a	----GA-A--T-TC----------T-G--C---------C--T------
HCV-TR	3b	----A----------T----------C--T-----T
GB809_4	4a	----GA-T--------G--------T-----C----------
GB116	4c	----TA-T--T----------T--C--C----------T------
GB215	4c	-----A-C--T----------T--C--C----------
GB358	4c	----GA-C--T-----G--------T-----C----------
GB809_2	4e	----GA-C-----C----------T--C--C---------C--T------
CAM600	4e	----GA-C--T----------C---------C--T------
CAMG22	4f	----GA-T----------C--T------
CAMG27	4f	----GA-A----------T------
GB549	4g	----GA-T----------T-----C---------C--T------
GB438	4h	----GA-C--T--C----------C--C-----C--T------

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Figure 4 - Continued 5

CAR4/1205	4i	----GA-C--T----------T----------
CAR4/901	4?	----GA-T-----C----------T----------
BE95	5a	----G--A------C----------TT-A--C----------
BE100	5a	----G-----T----------T--G----------
PC-3-1	5a	G TT A C
PC-3-8	5a	G C TT A C
PC-4-1	5a	G TT A C
PC-4-6	5a	G TT A C
PC-4/E1	5a	G S TT A C

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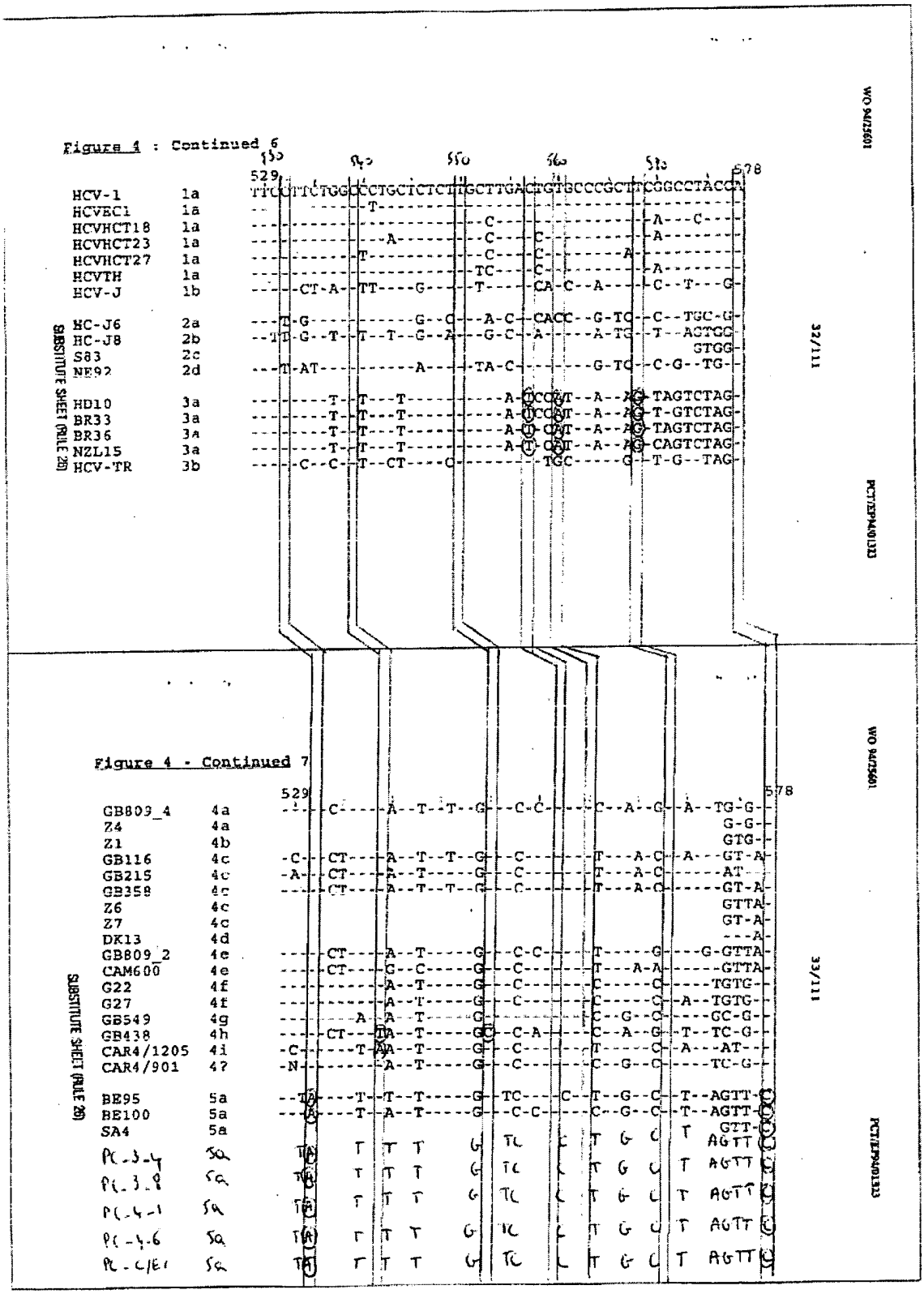
Figure 4 : Continued 6
529
578
HCV-1 1a
HCVEC1 1a
HCVHCT18 1a
HCVHCT23 1a
HCVHCT27 1a
HCVTH 1a
HCV-J 1b
HC-J6 2a
HC-J8 2b
S83 2c
NE92 2d
HD10 3a
BR33 3a
BR36 3a
NZL15 3a
HCV-TR 3b
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Figure 4 - Continued 7
529
578
GB809_4 4a
Z4 4a
Z1 4b
GB116 4c
GB215 4c
GB358 4c
Z6 4c
Z7 4c
DK13 4d
GB809_2 4e
CAM600 4e
G22 4f
G27 4f
GB549 4g
GB438 4h
CAR4/1205 4i
CAR4/901 4?
BE95 5a
BE100 5a
SA4 5a
PC-3-4 5a
PC-3-9 5a
PC-4-1 5a
PC-4-6 5a
PC-C/E1 5a
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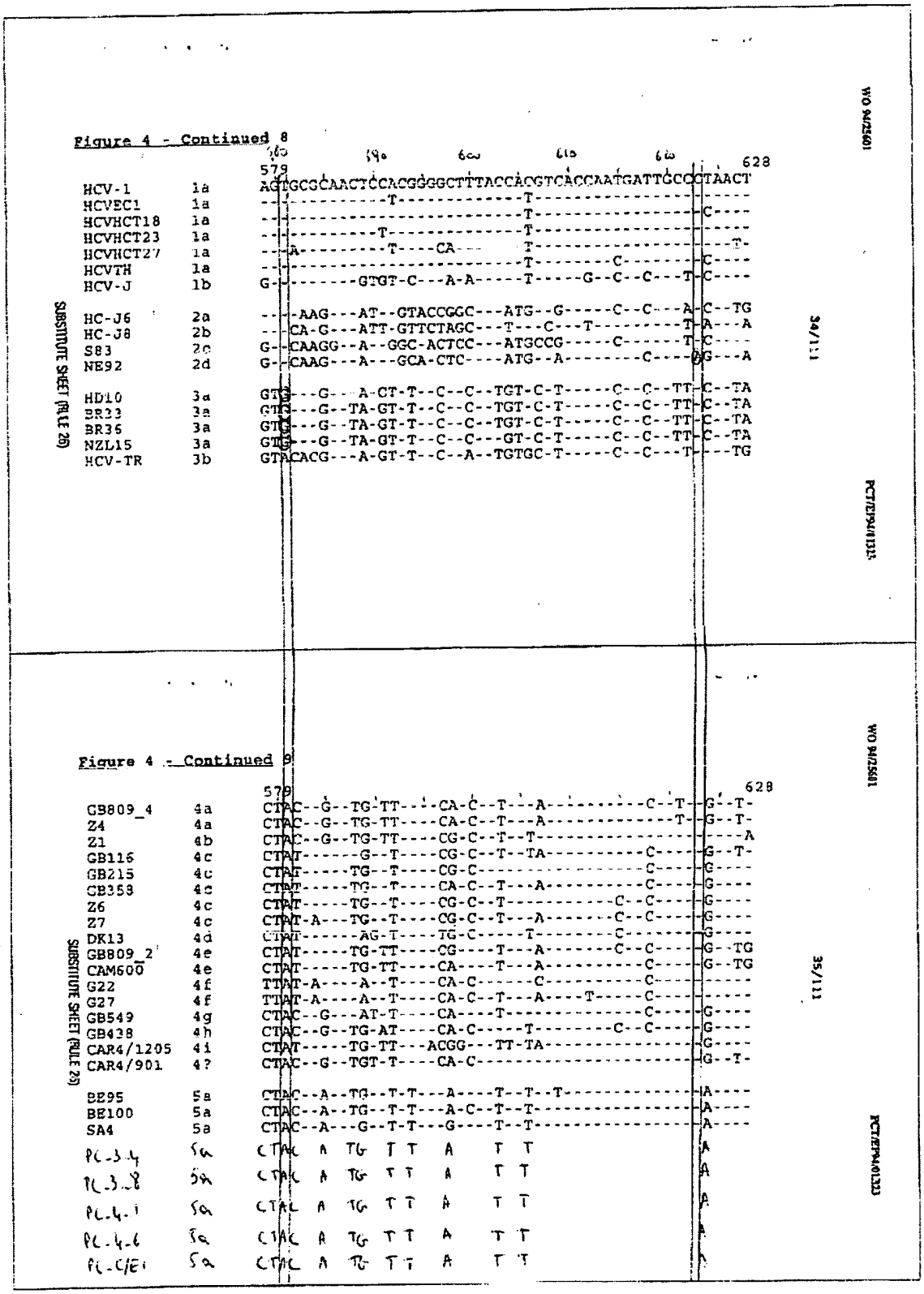
Figure 4 - Continued 8
579
628
HCV-1 1a AGTGCCCAACTCCACGGGGCTTTACCACGTCACCAATGATTGCCCTAACT
HCVEC1 1a
HCVHCT18 1a
HCVHCT23 1a
HCVHCT27 1a
HCVTH 1a
HCV-J 1b
HC-J6 2a
HC-J8 2b
S83 2c
NE92 2d
HD10 3a
BR33 3a
BR36 3a
NZL15 3a
HCV-TR 3b
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Figure 4 - Continued 9
579
628
GB809_4 4a
Z4 4a
Z1 4b
GB116 4c
GB215 4c
GB358 4c
Z6 4c
Z7 4c
DK13 4d
GB809_2 4e
CAM600 4e
G22 4f
G27 4f
GB549 4g
GB438 4h
CAR4/1205 4i
CAR4/901 4?
BE95 5a
BE100 5a
SA4 5a
PL-3.4 5a
PL-3.8 5a
PL-4.1 5a
PL-4.6 5a
PL-CIE1 5a
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Figure 4 - Continued 10

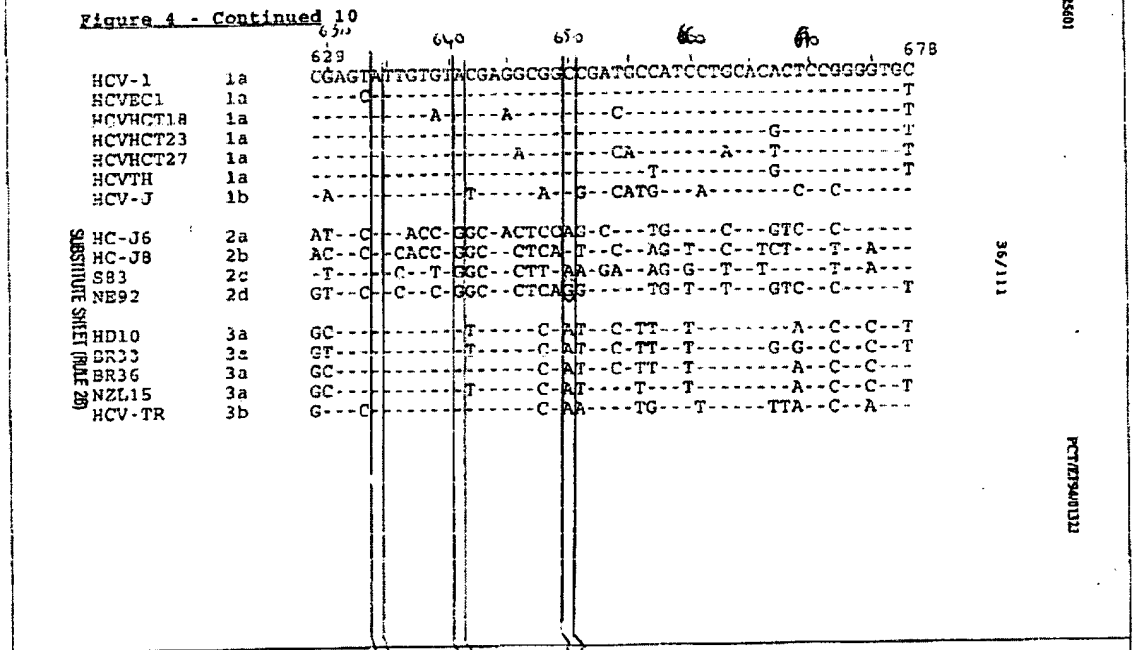
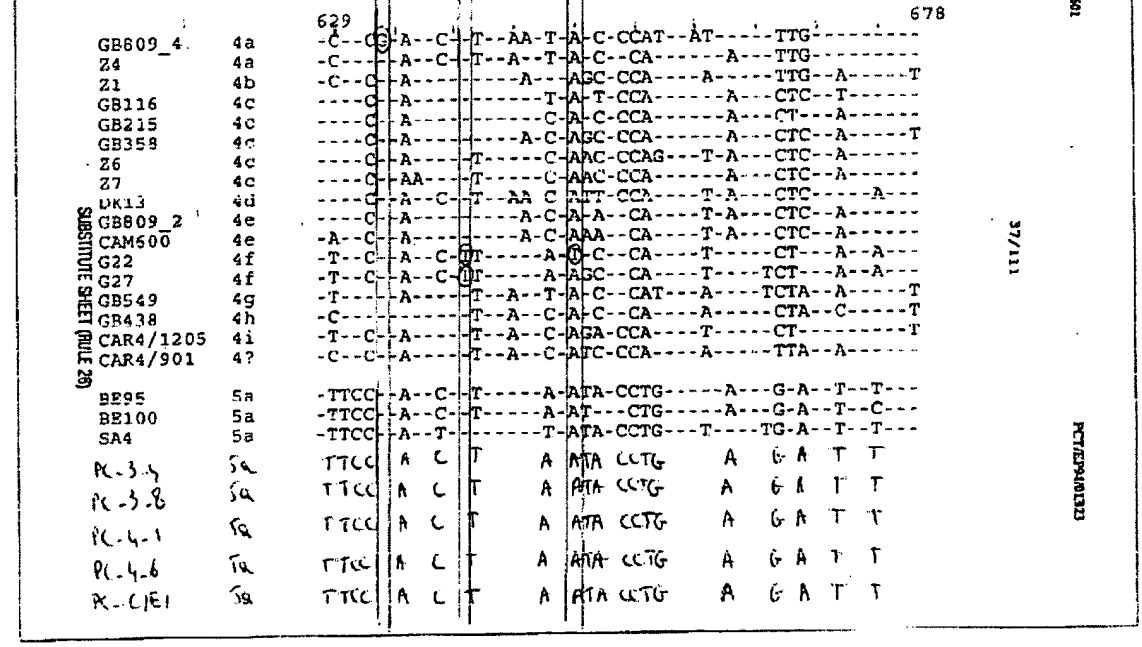


Figure 4 - Continued 11



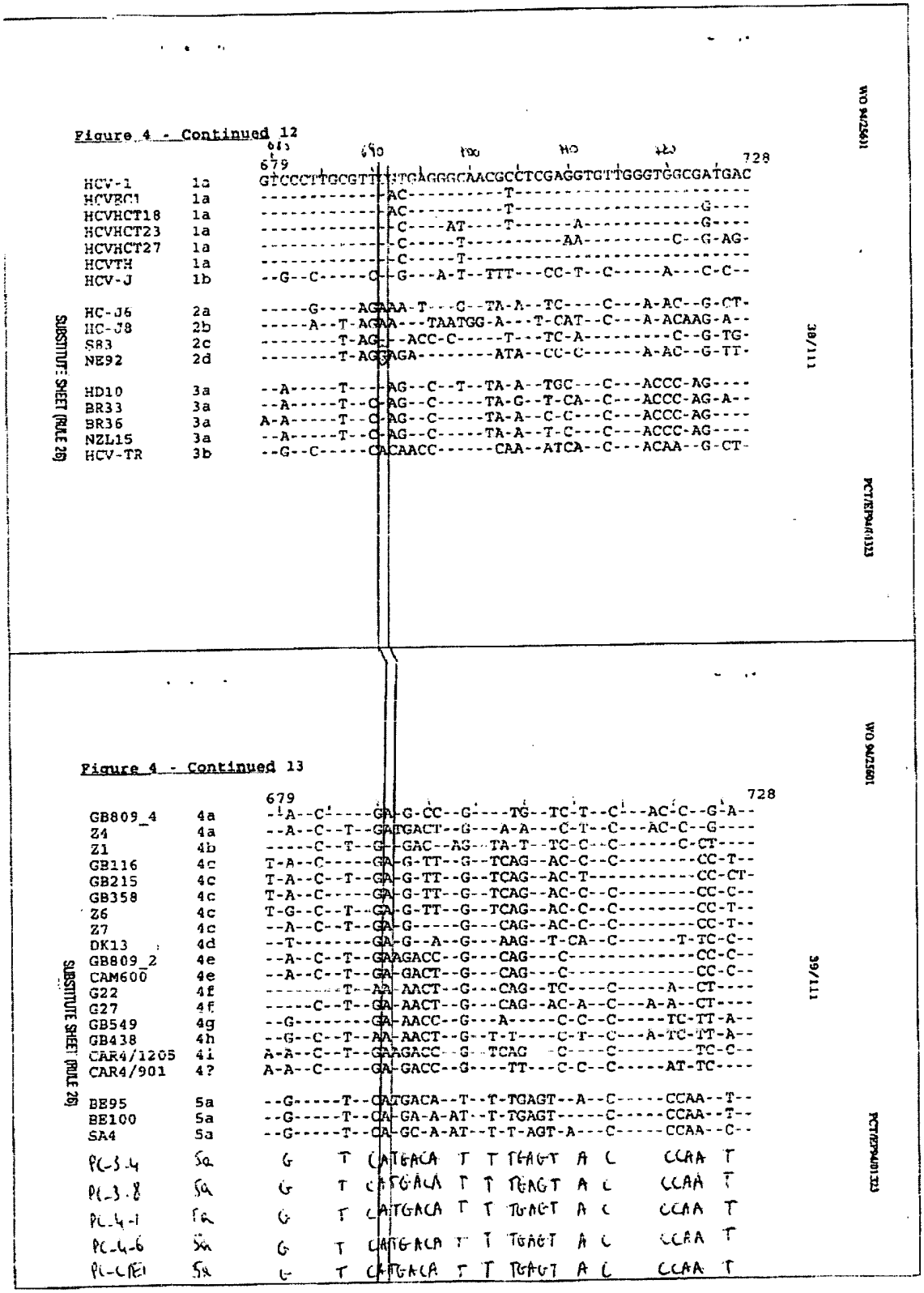


Figure 4 - Continued 12
679
728
HCV-1 1a GTCCCTTGCGTTCTGAGGGCAACGCCTCGAGGTGTTGGGTGGCGATGAC
HCVBC1 1a
HCVHCT18 1a
HCVHCT23 1a
HCVHCT27 1a
HCVTH 1a
HCV-J 1b
HC-J6 2a
HC-J8 2b
S83 2c
NE92 2d
HD10 3a
BR33 3a
BR36 3a
NZL15 3a
HCV-TR 3b
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Figure 4 - Continued 13
679
728
GB809_4 4a
Z4 4a
Z1 4b
GB116 4c
GB215 4c
GB358 4c
Z6 4c
Z7 4c
DK13 4d
GB809_2 4e
CAM600 4e
G22 4f
G27 4f
GB549 4g
GB438 4h
CAR4/1205 4i
CAR4/901 4?
BE95 5a
BE100 5a
SA4 5a
PC-3.4 5a
PC-3.8 5a
PC-4-1 5a
PC-4-6 5a
PC-CPE1 5a
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Figure 4 - Continued 14

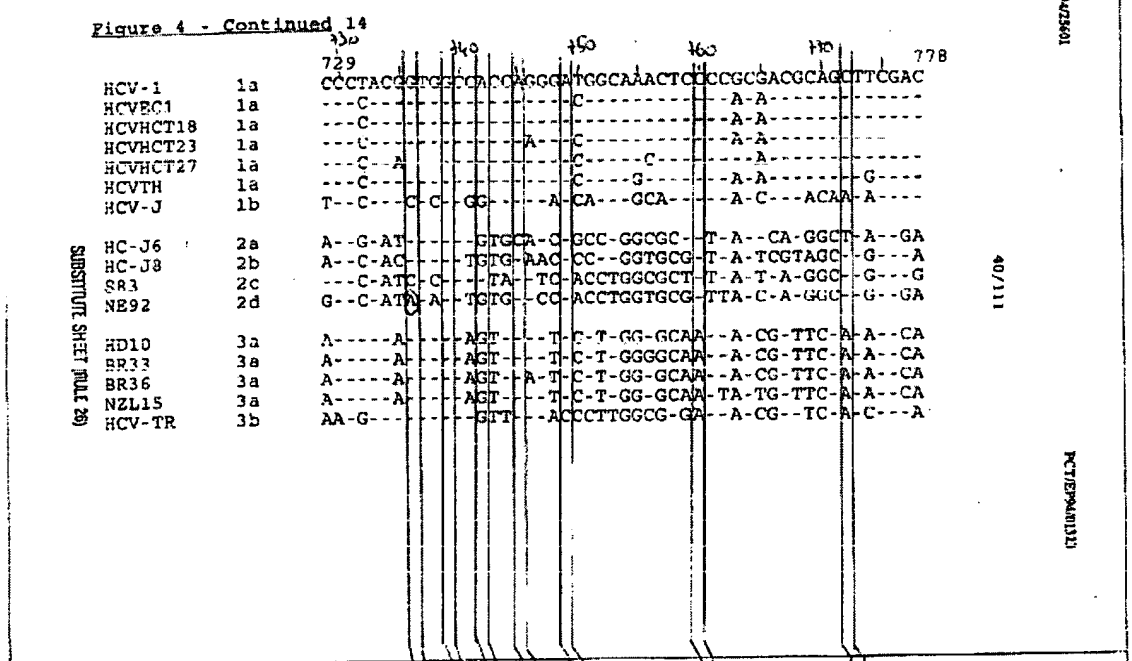
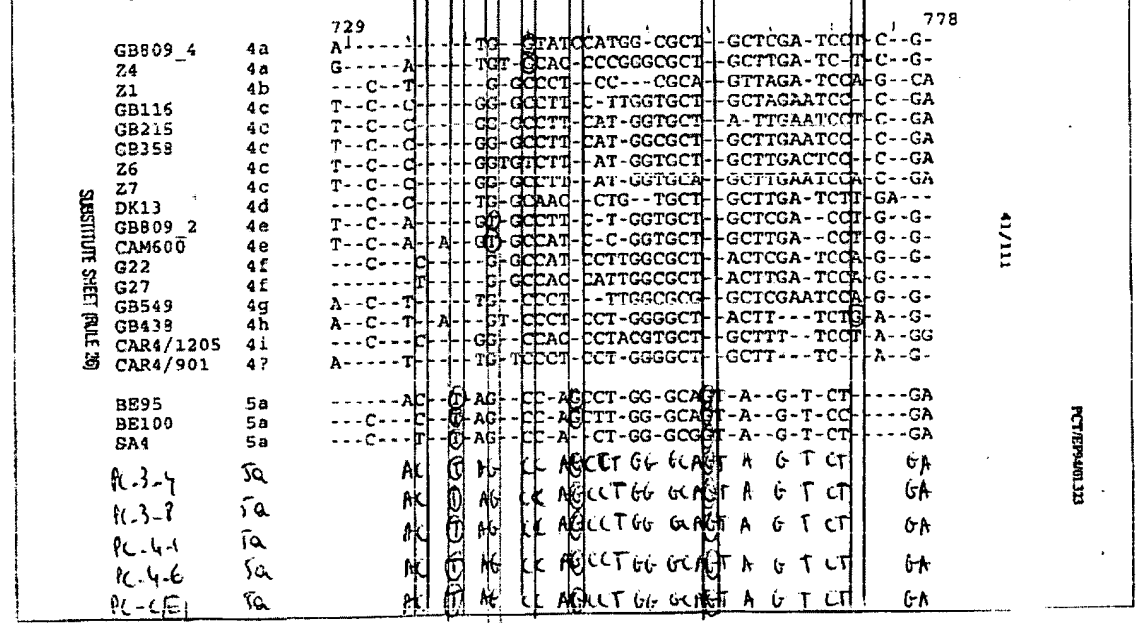


Figure 4 - Continued 15



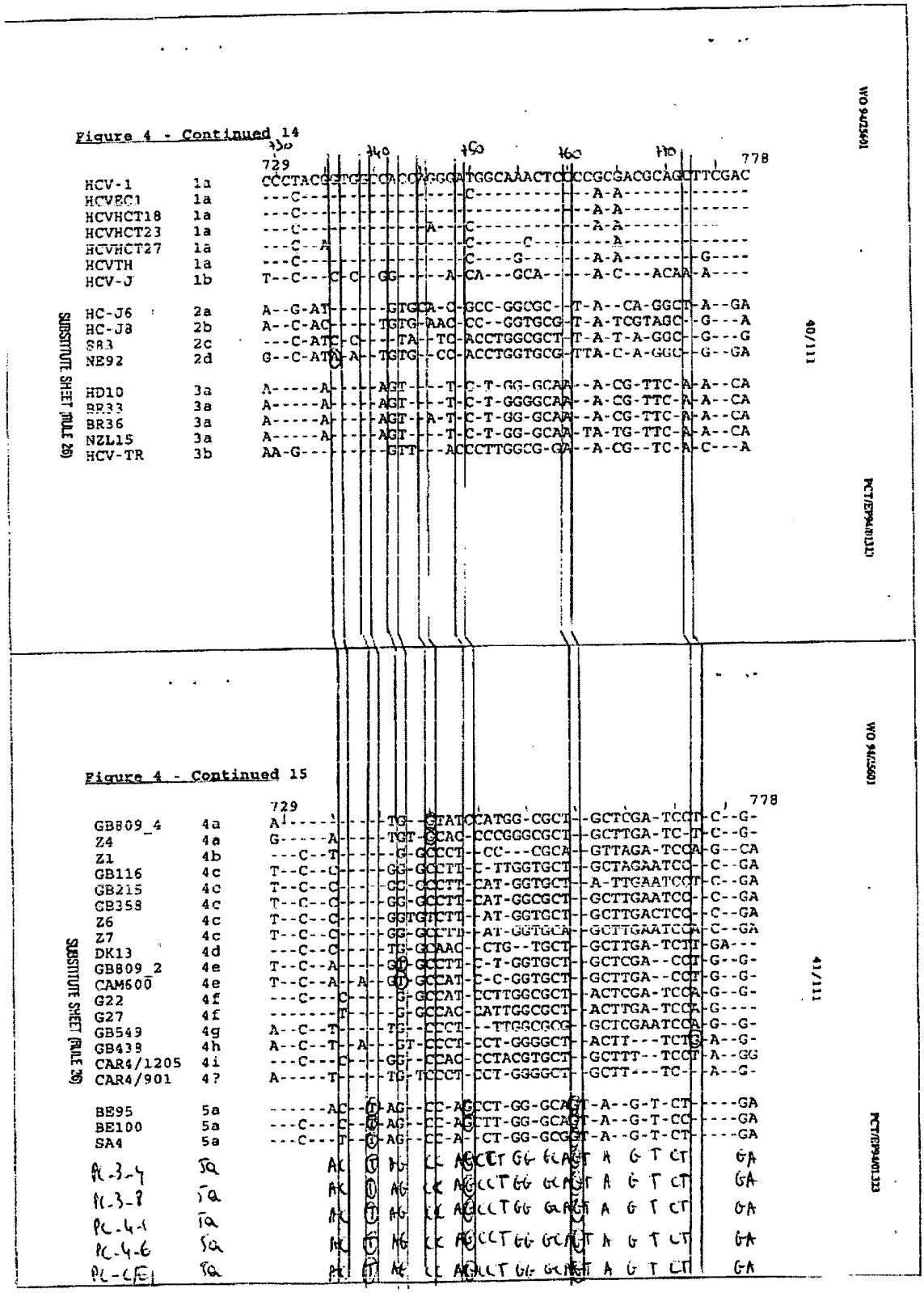

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Figure 4 - Continued 15
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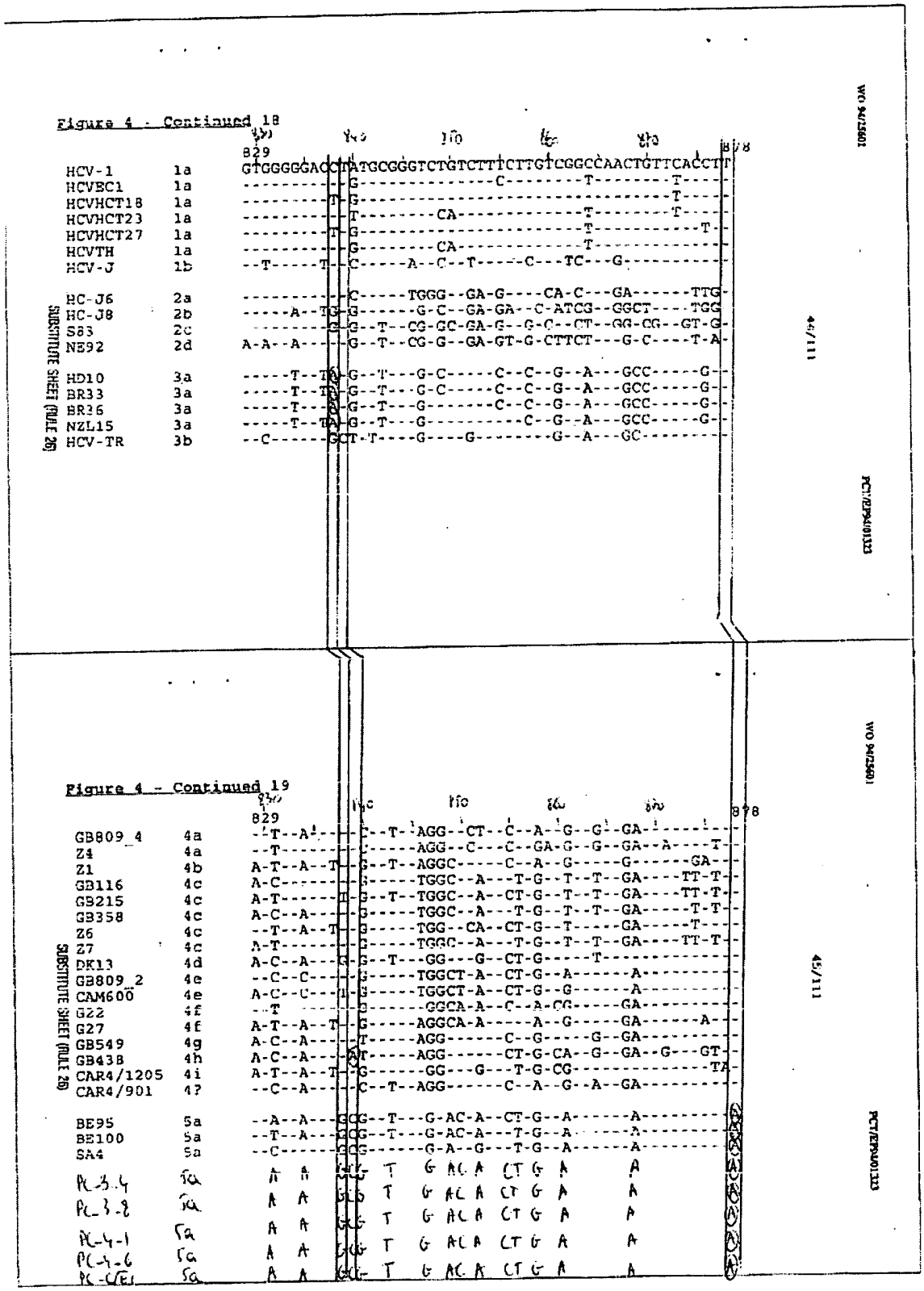
Figure 4 - Continued 18
Figure 4 - Continued 19
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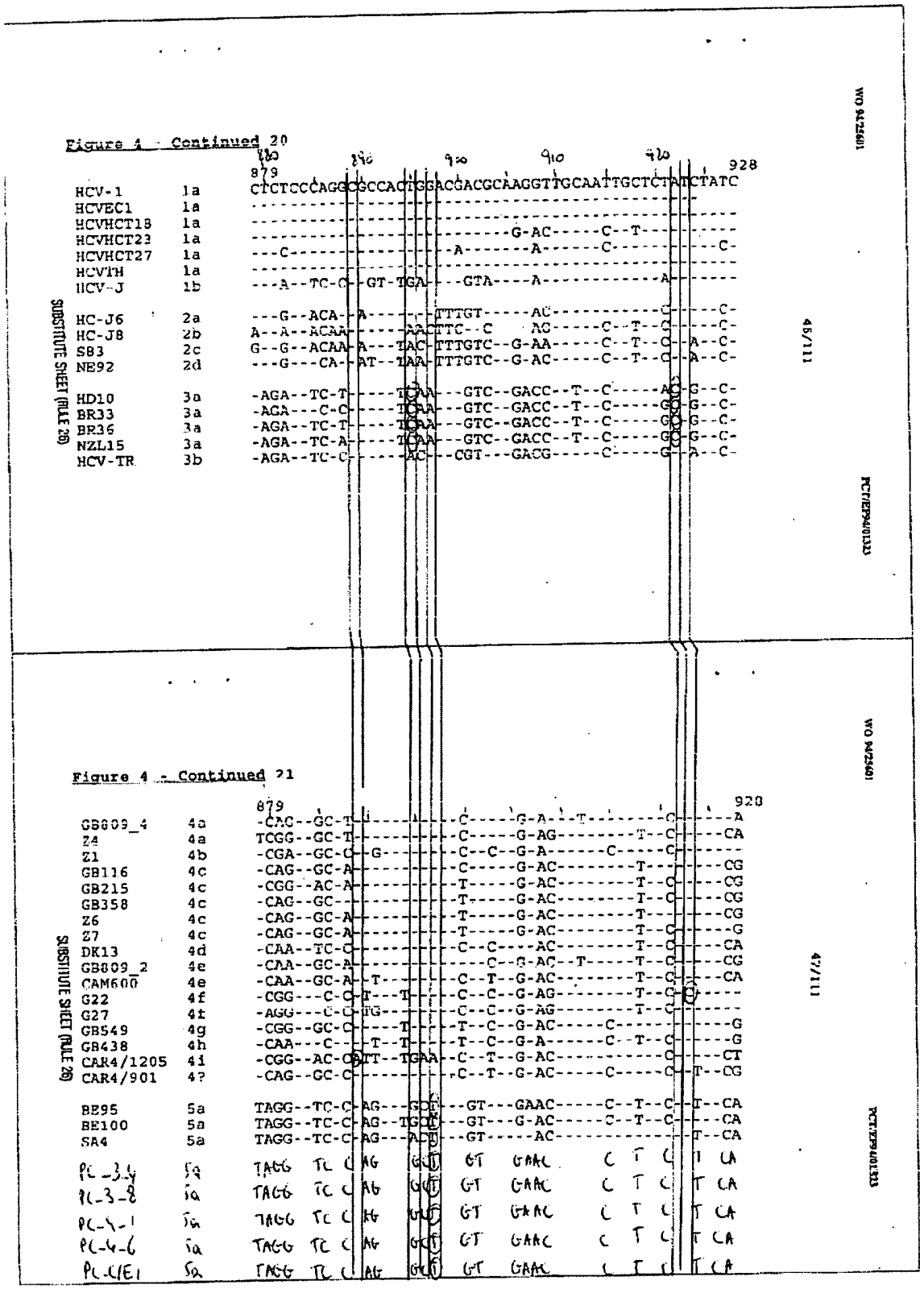
Figure 4 - Continued 20
879
928
HCV-1 1a CTCTCCCAGGCGCCACTGGACGACGCAAGGTTGCAATTGCTCTATCTATC
HCVEC1 1a
HCVHCT18 1a
HCVHCT23 1a
HCVHCT27 1a
HCVTH 1a
HCV-J 1b
HC-J6 2a
HC-J8 2b
SB3 2c
NE92 2d
HD10 3a
BR33 3a
BR36 3a
NZL15 3a
HCV-TR 3b
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Figure 4 - Continued 21
879
928
GB809_4 4a
Z4 4a
Z1 4b
GB116 4c
GB215 4c
GB358 4c
Z6 4c
Z7 4c
DK13 4d
GB809_2 4e
CAM600 4e
G22 4f
G27 4f
GB549 4g
GB438 4h
CAR4/1205 4i
CAR4/901 4?
BE95 5a
BE100 5a
SA4 5a
PC-3-4 5a
PC-3-8 5a
PC-4-1 5a
PC-4-6 5a
PC-C/E1 5a
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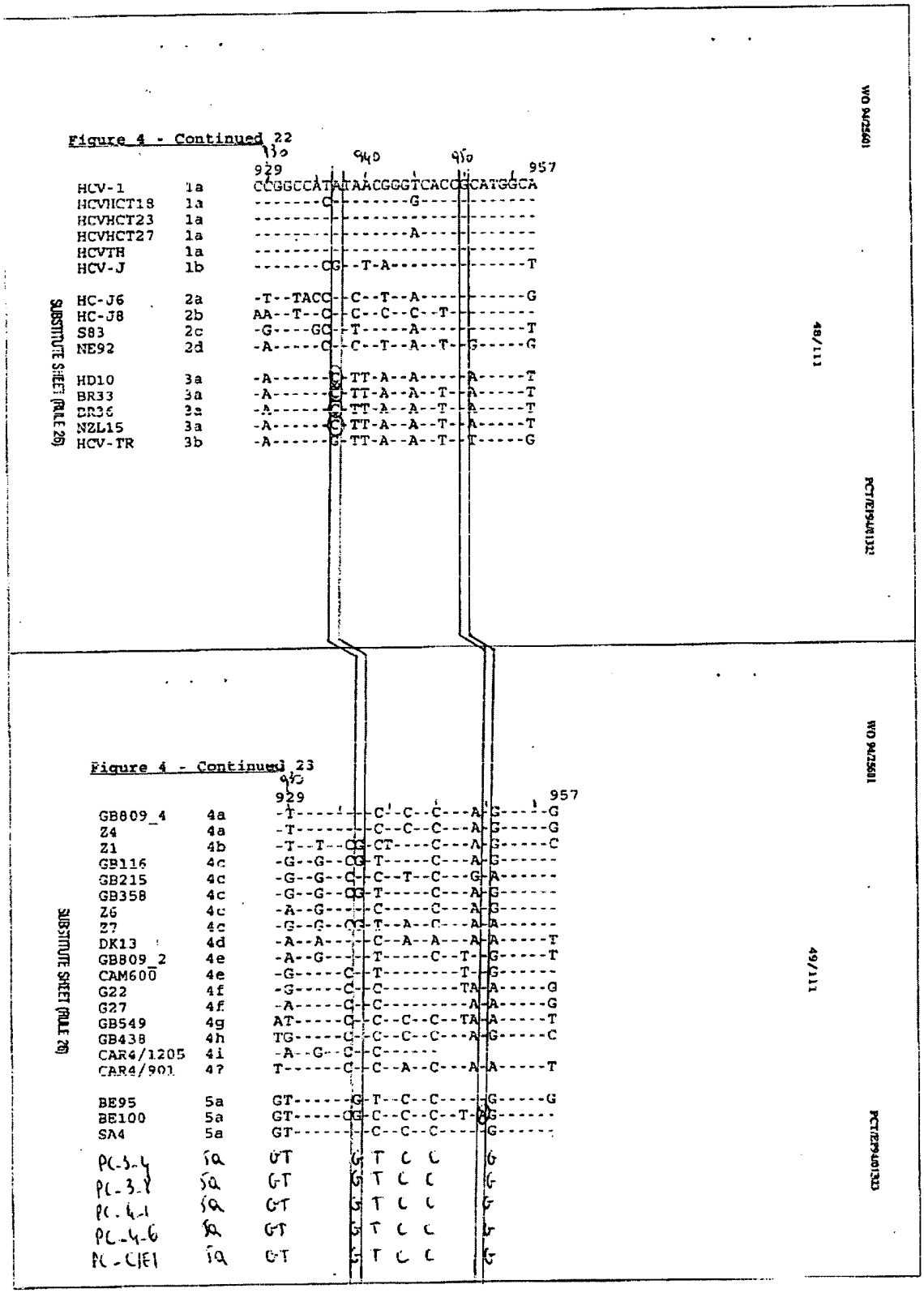
Figure 4 - Continued 22
929
957
HCV-1 1a CCGGCCATAATAACGGGTCACCGCATGGCA
HCVHCT18 1a -------C---------G----------
HCVHCT23 1a ----------------------------
HCVHCT27 1a ----------------A----------
HCVTH 1a ----------------------------
HCV-J 1b -------CG--T-A----------T
HC-J6 2a -T--TACC--C--T--A----------G
HC-J8 2b AA--T--C--C--C--C--T---------
S83 2c -G----GC--T-----A----------T
NE92 2d -A-----C--C--T--A--T--G-----G
HD10 3a -A------C-TT-A--A-----A-----T
BR33 3a -A------C-TT-A--A--T--A-----T
BR36 3a -A------C-TT-A--A--T--A-----T
NZL15 3a -A------C-TT-A--A--T--A-----T
HCV-TR 3b -A------G-TT-A--A--T--T-----G
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Figure 4 - Continued 23
929
957
GB809_4 4a -T-------C--C--C---A-G-----G
Z4 4a -T----------C--C--C---A-G-----G
Z1 4b -T--T--CG-CT----C---A-G-----C
GB116 4c -G--G--CG-T-----C---A-G------
GB215 4c -G--G--C--C--T--C---G-A------
GB358 4c -G--G--CG-T-----C---A-G------
Z6 4c -A--G-------C-----C---A-G------
Z7 4c -G--G--C--T--A--C---A-A------
DK13 4d -A--A-------C--A--A---A-A-----T
GB809_2 4e -A--G-------T-----C--T--G-----T
CAM600 4e -G-----C--T---------T--G------
G22 4f -G-----C--C---------TA-A-----G
G27 4f -A-----C--C---------A-A-----G
GB549 4g AT-----C--C--C--C--TA-A-----T
GB438 4h TG-----C--C--C--C---A-G-----C
CAR4/1205 4i -A--G--C--C------
CAR4/901 4? T------C--C--A--C---A-A-----T
BE95 5a GT------G-T--C--C-----G-----G
BE100 5a GT-----CG-C--C--C--T-G------
SA4 5a GT-------C--C--C-----G------
PC-3-4 5a GT T C C G
PC-3-7 5a GT T C C G
PC-4-1 5a GT T C C G
PC-4-6 5a GT T C C G
PC-CIE1 5a GT T C C G
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Withdrawal of the Section 112, first paragraph, rejection of the claims stated on pages 2-5 of the Office Action dated September 23, 2005, is requested.

The Section 112, first paragraph "written description", rejection of claims 24-57 stated on page 4 of the Office Action of September 23, 2005, is submitted to be obviated by the above amendments. Reconsideration and withdrawal of the rejection are requested as the claims do not require hybridization, as suggested by the Examiner's reference to "desired properties" as a basis of the rejection. Entry of the above amendments and withdrawal of the rejection are requested.

The present Amendment is submitted to place the application in condition for allowance without raising new issues requiring further search and/or consideration. No new matter has been added. Entry of the present Amendment and allowance of the application are requested.

The Examiner is requested to contact the undersigned in the event anything further is required.

Respectfully submitted,

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By: _____
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Reg. No. 36,663

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